PRECIS

Adult patients with myelodysplasia, leukemia, and non-Hodgkin's lymphoma can be cured by allogeneic bone marrow transplantation(BMT). This curative effect has until now been ascribed to the intense chemoradiotherapy used to condition the recipient for transplantation. The assumption that the curative effect of allogeneic transplantation rests in the ability to deliver very high doses of chemoradiotherapy has led to the restriction of allogeneic transplantation to those recipient patients whose overall status would permit the use of such intense conditioning. As a result, HIV positivity has generally appeared as an exclusion criteria to allogeneic transplantation for hematologic malignancies. Additionally, early studies of allogeneic BMT in HIV patients suggested no benefit in controlling the progression to AIDS.

Several in vitro studies have demonstrated the existence of donor derived CD4 and CD8 positive lymphocytes with specific reactivity to recipient leukemia providing a potent graft versus leukemia (GVL) effect, and this GVL effect is area of intense interest both at the NIH and elsewhere. In fact, early attempts to decrease treatment related mortality in chronic myelogenous leukemia(CML) patients undergoing allogeneic BMT by T-cell depletion of the graft resulted in an unacceptably high rate of relapse suggesting that alloreactivity in the donor graft accounted for a significant portion of the cure rate in this disease. This GVL effect is most dramatically demonstrated among relapsed allogeneic bone marrow transplant recipients transplanted for CML in whom a simple infusion of donor lymphocytes can induce a complete and durable remission.

Non-myeloablative allogeneic peripheral blood stem cell transplants are currently being investigated for engraftment efficacy and toxicity in a number of transplant centers. Preliminary data including our own experience with 13 patients undergoing this type of procedure have shown a high rate of complete donor engraftment, low toxicity, and preservation of the GVL effect. Two recent published studies investigating non-myeloablative allo-transplantation in standard risk patients revealed an extremely low rate of transplant related complications and mortality.

The decreased risk of transplant related complications associated with non-myeloablative transplants expands the eligibility of transplant candidates and may allow successful application in patients infected with HIV. In this study, we will assess the safety and efficacy of nonmyeloablative transplantation in patients with HIV infection. Moreover, the introduction of an HIV resistance vector into a portion of the allogeneic graft provides a unique opportunity to test the in vivo efficacy of introducing resistance to HIV through the self renewing stem cell.

The end points of this study are engraftment, degree of donor-host chimerism, incidence of acute and chronic GVHD, transplant related morbidity and mortality, disease free survival, as well as overall survival, and overall level and persistence of progeny of gene modified cells.